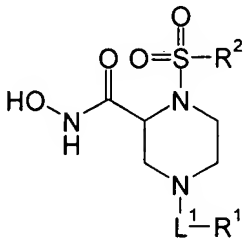
AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the Application.

LISTING OF CLAIMS

1. (currently amended) A compound of structural formula **I**:



I

and pharmaceutically acceptable salts~~, esters, amides, and prodrugs~~ thereof wherein

L^1 is -C(O)-, -$S(O)_2$-, or -$(CH_2)_n$-;

R^1 is –H, -OR^{11}, -$(CH_2)_nR^{11}$, -$C(O)R^{11}$, or -$NR^{12}R^{13}$;

R^{11}, R^{12}, and R^{13} independently are

a) R^{50};

b) saturated or mono- or poly- unsaturated C_5-C_{14}-mono- or fused poly-cyclic hydrocarbyl, optionally containing one or two annular heteroatoms per ring and optionally substituted with one or two R^{50} substituents;

c) C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, or -C(O)H, each of which is optionally substituted with one, two or three substituents independently selected from R^{50} and saturated or mono- or poly- unsaturated C_5-C_{14}-mono- or fused poly- cyclic hydrocarbyl, optionally containing one or two annular heteroatoms per ring and optionally substituted with one, two or three R^{50} substituents;

or R^{12} and R^{13} together with the N to which they are covalently bound, a C_5-C_6 heterocycle optionally containing a second annular heteroatom and optionally substituted with one or two R^{50} substituents;

R^2 is -R^{21}-L^2-R^{22};

R^{21} is saturated or mono- or poly- unsaturated C_5-C_{14}-mono- or fused poly- cyclic hydrocarbyl, optionally containing one or two annular heteroatoms per ring and optionally substituted with one, two, or three R^{50} substituents;

L^2 is -O-, -C(O)-, $-CH_2$-, -NH-, $-S(O_2)$- or a direct bond;

R^{22} is saturated or mono- or poly- unsaturated C_5-C_{14}-mono- or fused poly- cyclic hydrocarbyl, optionally containing one or two annular heteroatoms per ring and optionally substituted with one, two, or three R^{50} substituents; and

R^{50} is R^{51}-L^3-$(CH_2)_n$-;

L^3 is -O-, -NH-, $-S(O)_{0-2}$-, -C(O)-, -C(O)O-, -C(O)NH-, -OC(O)-, -NHC(O)-, $-C_6H_4$-, or a direct bond;

R^{51} is -H, C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, halo, $-CF_3$, $-OCF_3$, -OH, $-NH_2$, mono-C_1-C_6alkyl amino, di-C_1-C_6alkyl amino, -SH, $-CO_2H$, -CN, $-NO_2$, $-SO_3H$, or a saturated or mono- or poly- unsaturated C_5-C_{14}-mono- or fused poly- cyclic hydrocarbyl, optionally containing one or two annular heteroatoms per ring and optionally substituted with one, two, or three substituents;

wherein n is 0, 1, 2, or 3;

provided that an O or S is not singly bonded to another O or S in a chain of atoms.

2. (original) The compound according to claim 1, wherein L^1 is -C(O)- or $-S(O)_2$-.

3. (original) The compound according to claim 2, wherein L^1 is -C(O)- and R^1 is $-OR^{11}$ or $-(CH_2)_nR^{11}$, $-OC_1$-C_6alkyl-mono-C_1-C_6alkyl amino, $-OC_1$-C_6alkyl-di-C_1-C_6alkyl amino, $-OC_1$-C_6alkyl-N-heterocyclyl, $-C_1$-C_6alkyl-mono-C_1-C_6alkyl amino, $-C_1$-C_6alkyl-di-C_1-C_6alkyl amino, or $-C_1$-C_6alkyl-N-heterocyclyl.

4. (original) The compound according to claim 2, wherein, R^1 is C_1-C_6-alkoxy-C_1-C_6-alkoxy.

5. (original) The compound according to claim 2, wherein R^1 is methoxyethoxy.

6. (original) The compound according to claim 3, wherein L^1 is $-S(O)_2$-, and R^1 is $-NR^{12}R^{13}$, $-(CH_2)_nR^{11}$, $-C_1$-C_6alkyl-mono-C_1-C_6alkyl amino, $-C_1$-C_6alkyl-di-C_1-C_6alkyl amino, or $-C_1$-C_6alkyl-N-heterocyclyl.

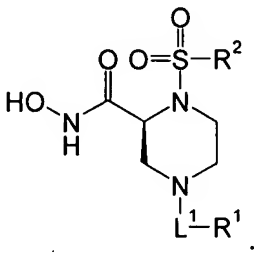
7. (original) The compound according to claim 3, wherein L^2 is -O-.

8. (original) The compound according to claim 7, wherein, R^2 is phenoxyphenyl wherein each phenyl is optionally substituted with one or two R^{50} substituents. In a more specific example, the R^{50} substituents are halo.

9. (original) The compound according to claim 8, wherein the saturated or mono- or poly-unsaturated C_5-C_{14}-mono- or fused poly- cyclic hydrocarbyl containing one or two annular heteroatoms per ring is selected from the group consisting of morpholinyl, piperazinyl, homopiperazinyl, pyrrolidinyl, piperidinyl, homopiperidinyl, furyl, thienyl, pyranyl, isobenzofuranyl, chromenyl, pyrrolyl, imidazolyl, isoxazolyl, pyridyl, pyrazinyl, pyrimidinyl, oxadiazolyl, indolyl, quinolinyl, carbazolyl, acrydinyl, and furazanyl, optionally substituted with one or two R^{50} substituents.

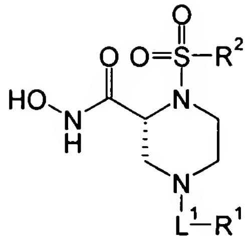
10. (original) The compound according to claim 8, wherein R^{12} and R^{13}, together with the N to which they are covalently bound, form a heterocycle selected from the group consisting of morpholinyl, piperazinyl, homopiperazinyl, pyrrolidinyl, piperidinyl, homopiperidinyl, pyrrolyl, imidazolyl, isoxazolyl, pyridyl, pyrazinyl, pyrimidinyl, oxadiazolyl, indolyl, quinolinyl, carbazolyl, acrydinyl, and furazanyl, optionally substituted with one or two R^{50} substituents.

11. (original) The compound according to claim 1, comprising the absolute stereochemistry of structural formula **II**:



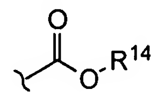
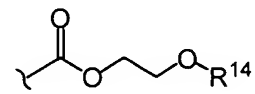
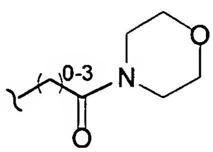
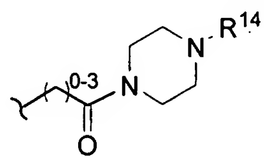
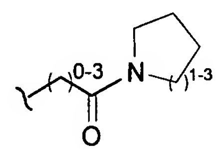
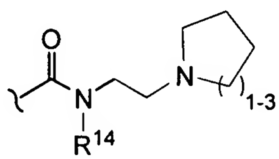
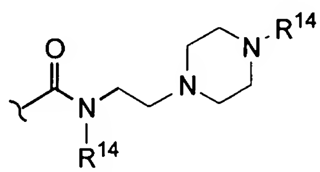
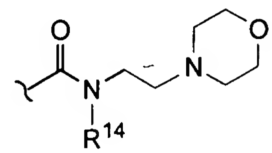
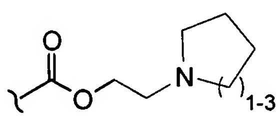
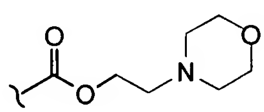
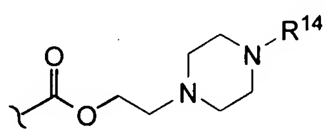
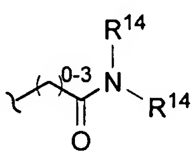
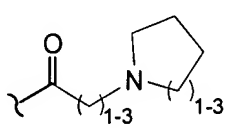
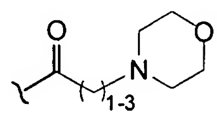
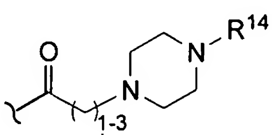
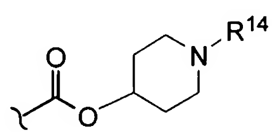
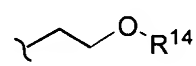
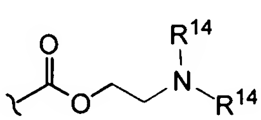
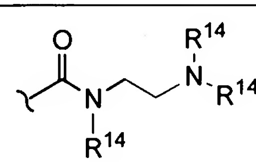
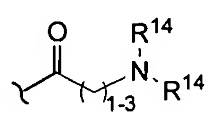
II

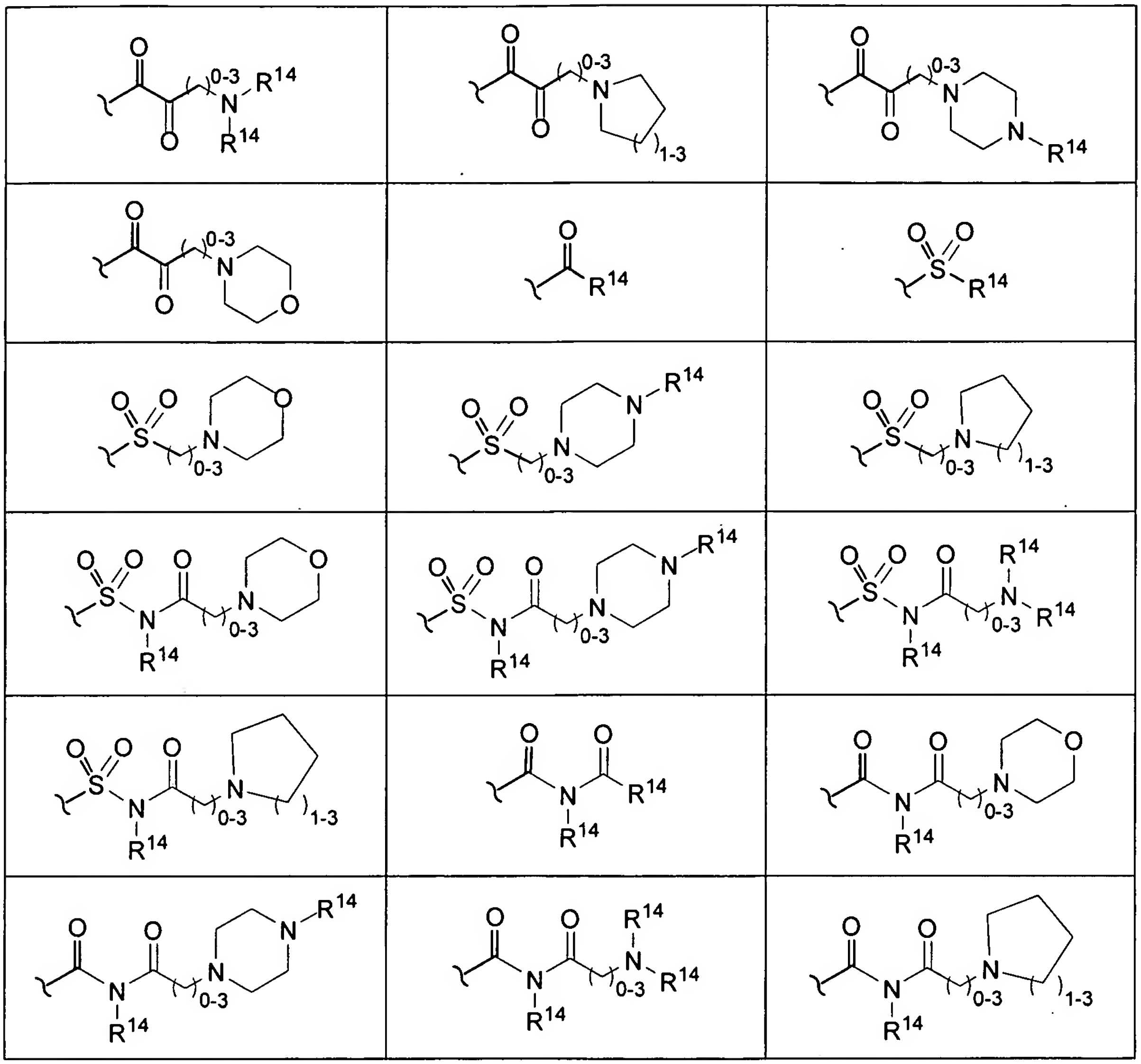
12. (original) The compound according to claim 1, comprising the absolute stereochemistry of structural formula **III**:



III

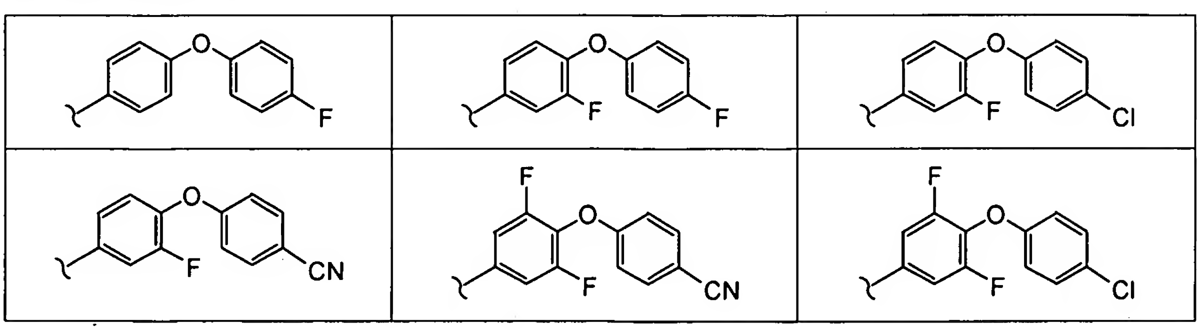
13. (original) The compound according to claim 1, wherein $-L^1-R^1$ is selected from:

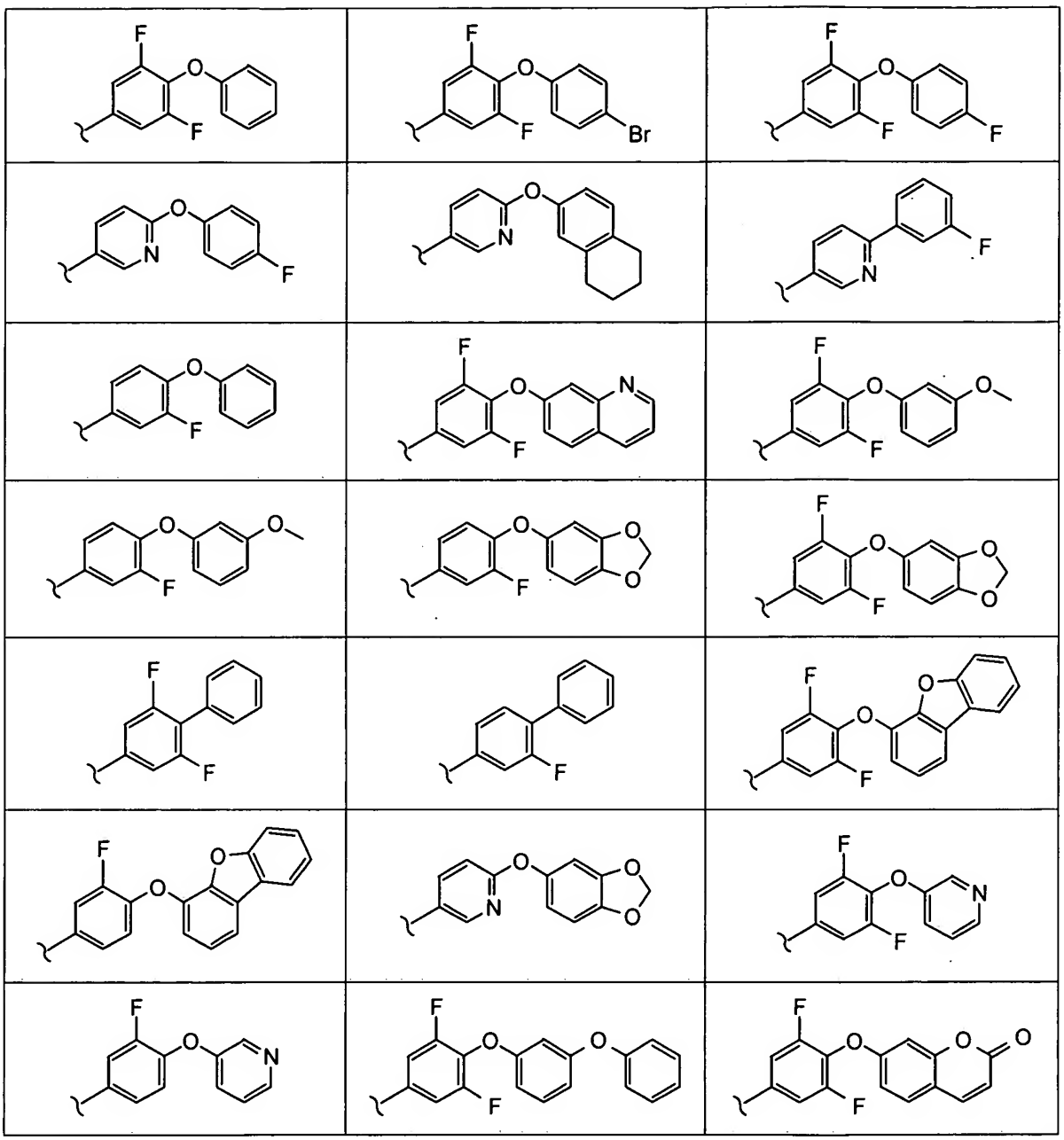
$-R^{14}$		
		
		
		
		
		
		



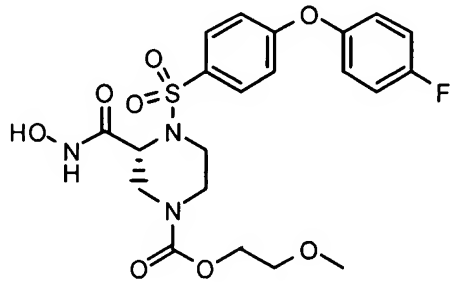
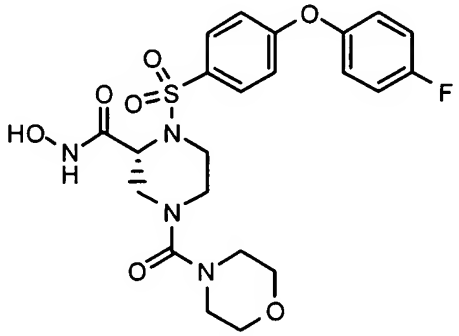
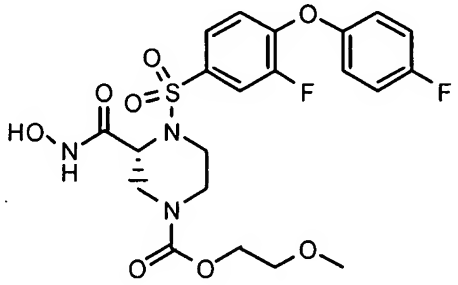
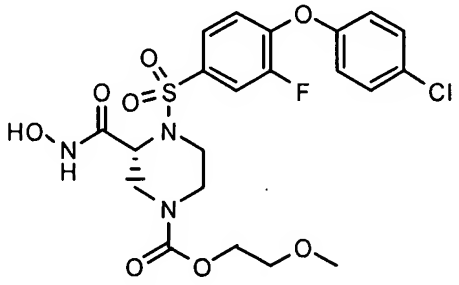
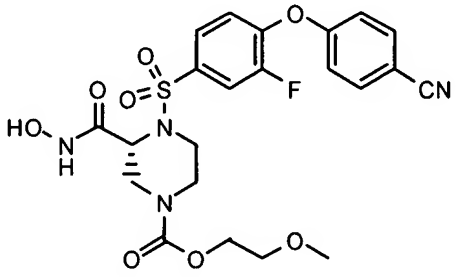
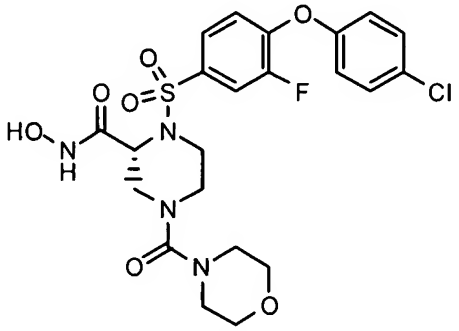
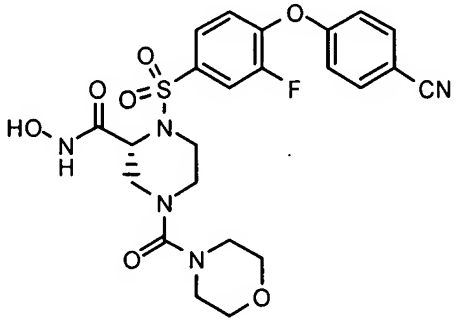
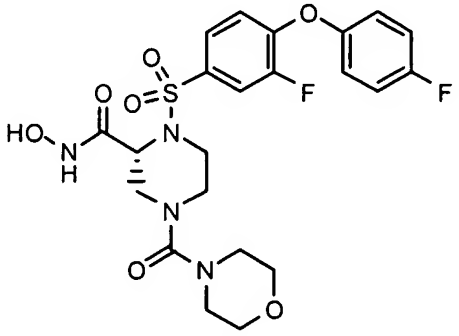
wherein each R^{14} is independently selected from –H, -$(CH_2)_{1\text{-}3}CO_2H$, alkyl, alkoxy, alkenyl, aryl, heteroaryl, arylalkyl, and heteroarylalkyl; and

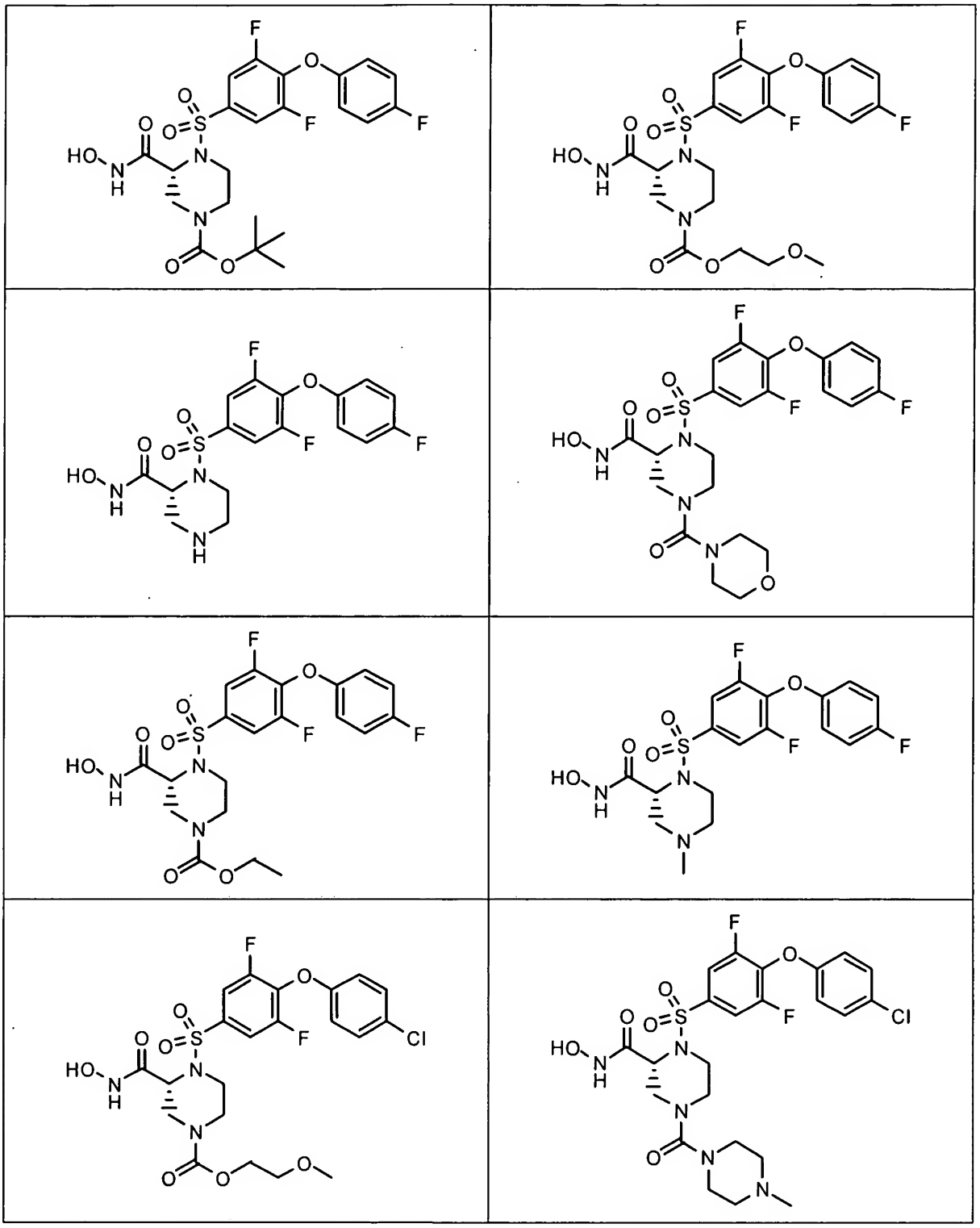
R^2 is selected from:

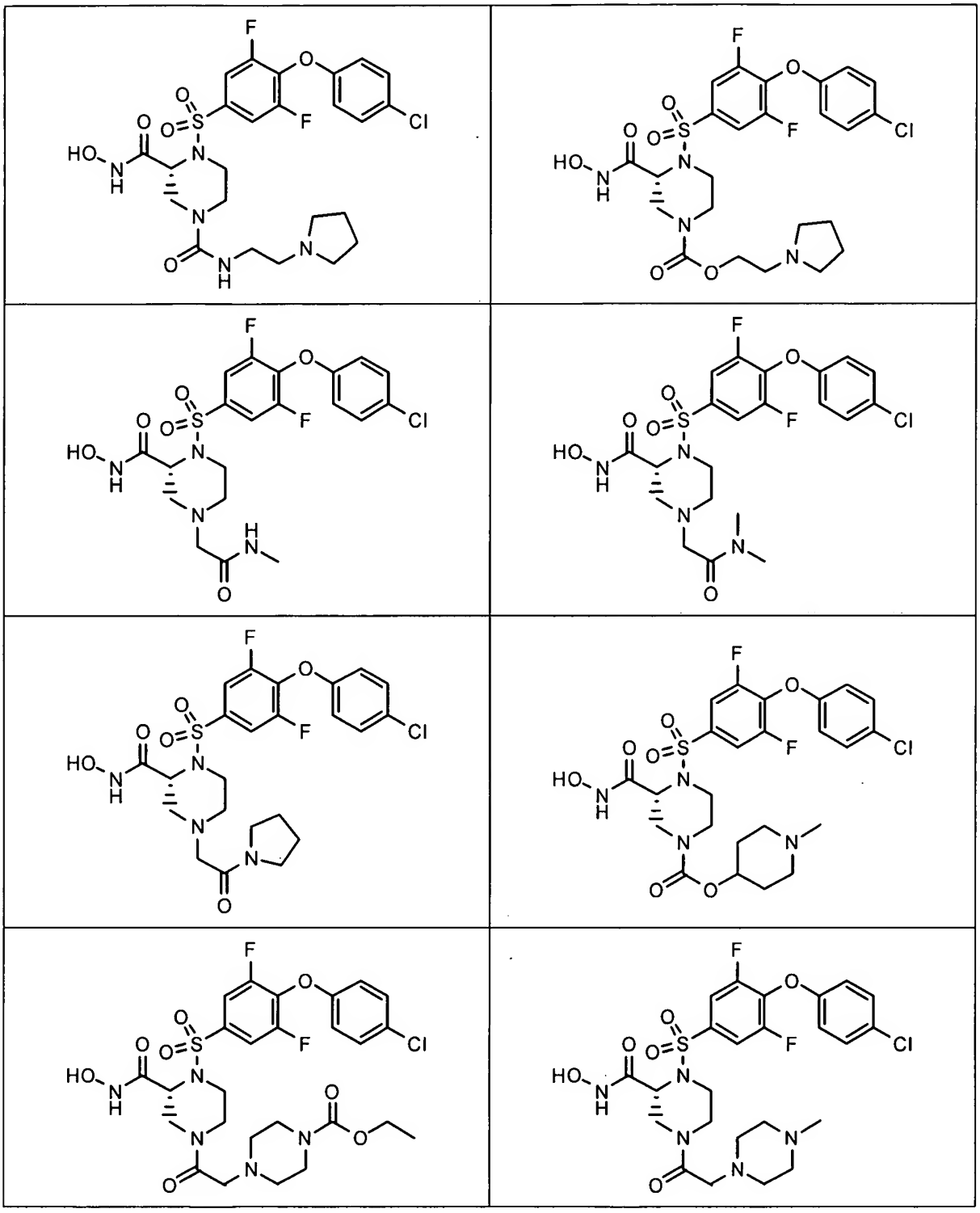


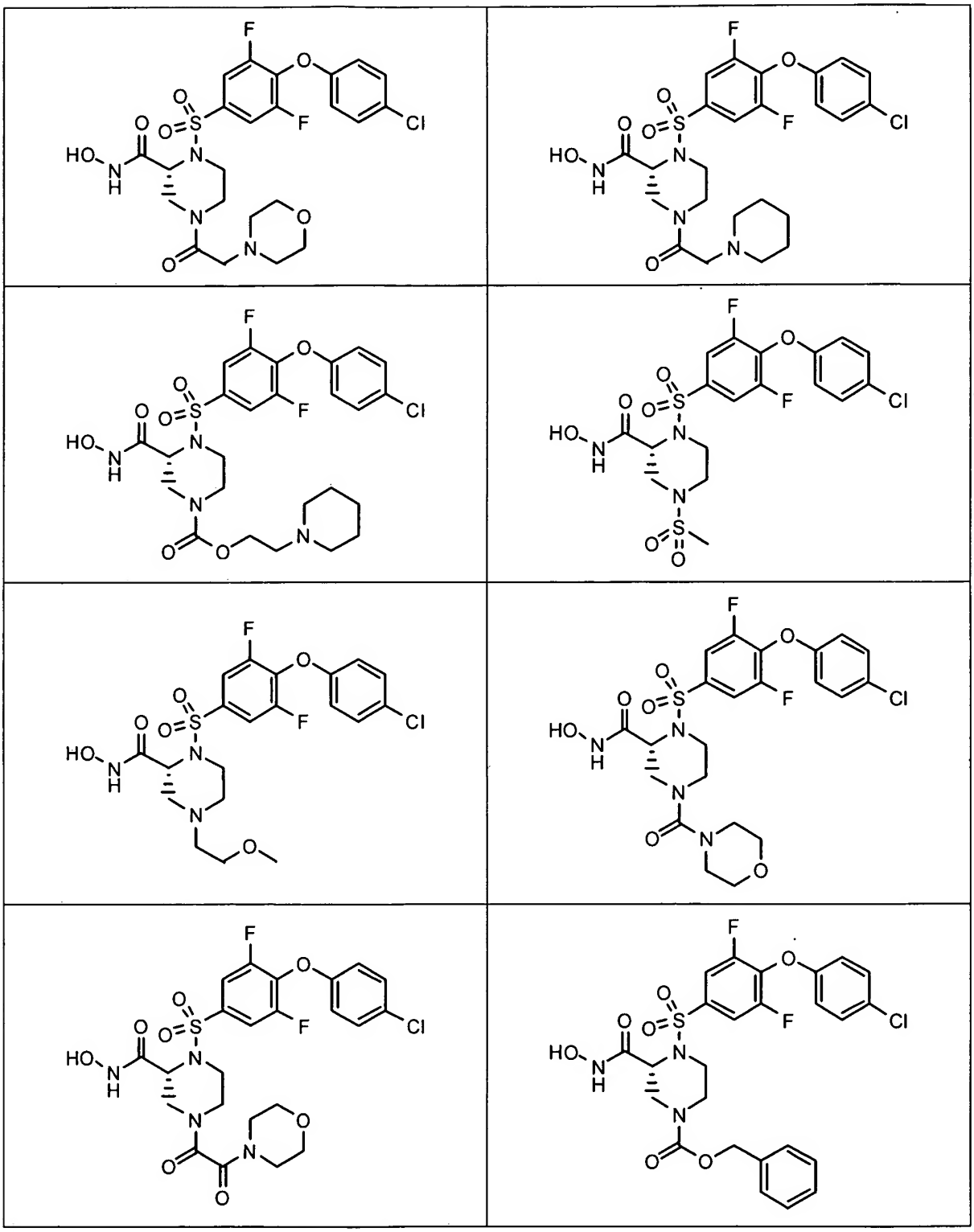


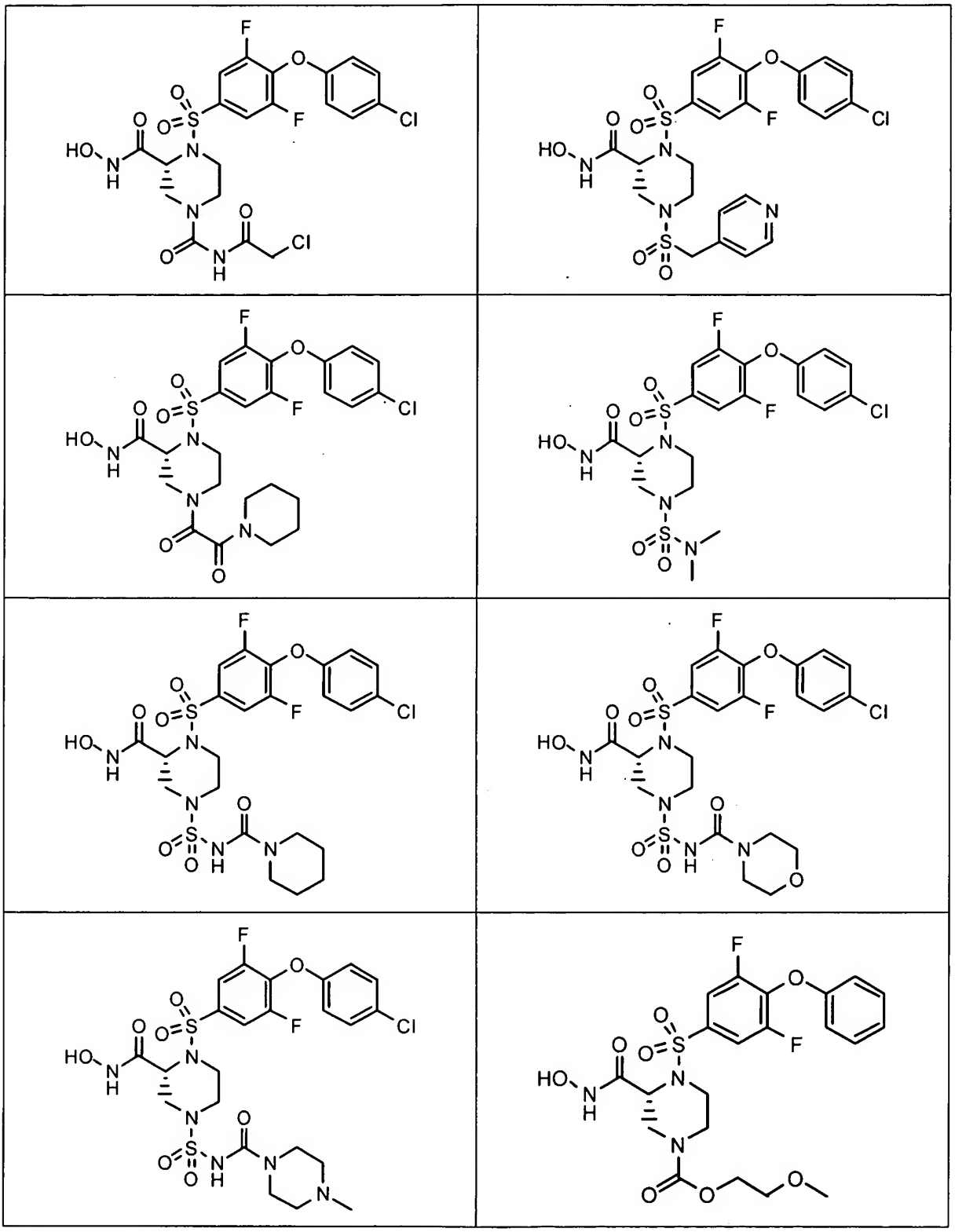
14. (original) The compound according to claim 1, selected from:

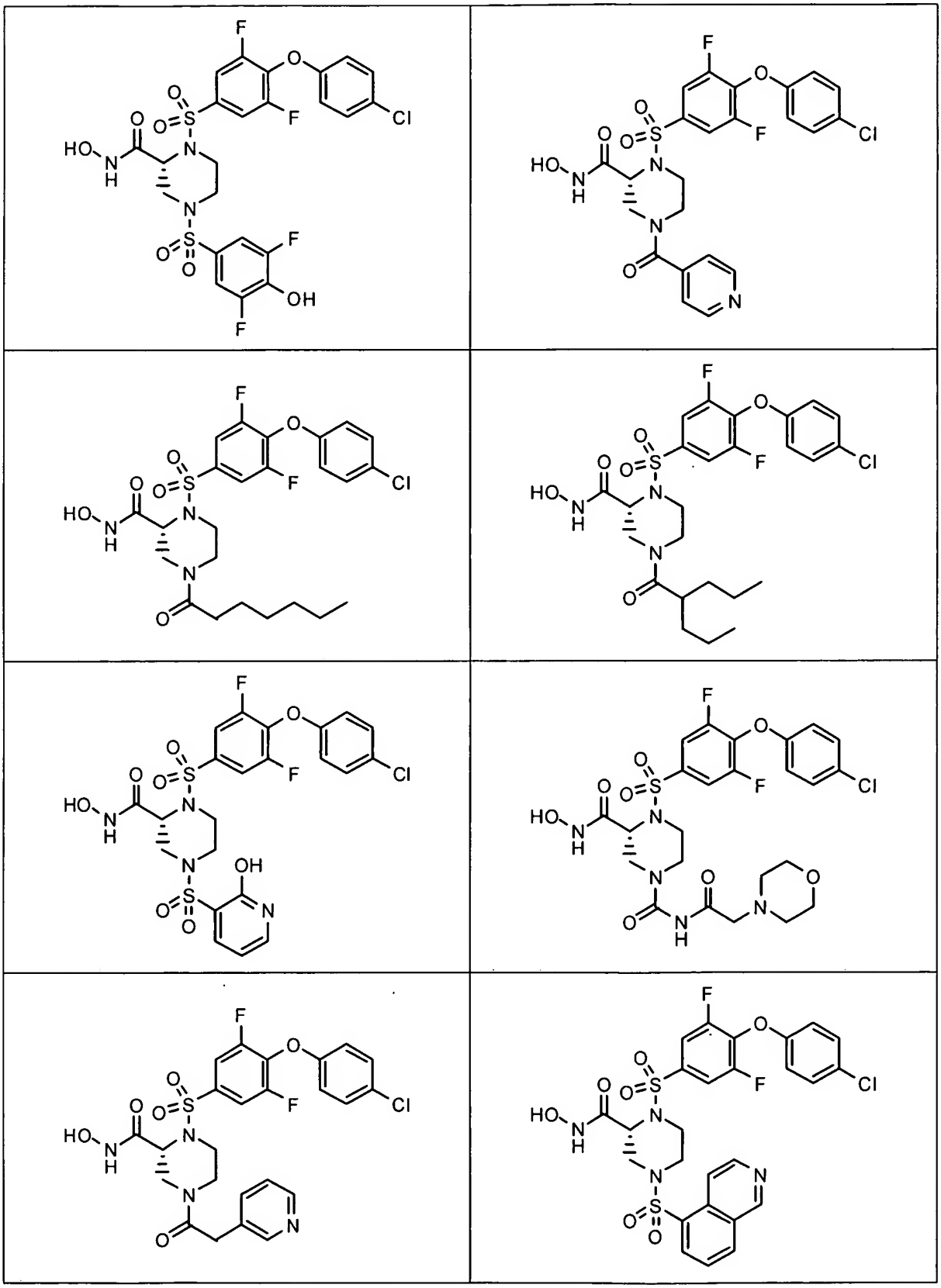
	
	
	
	

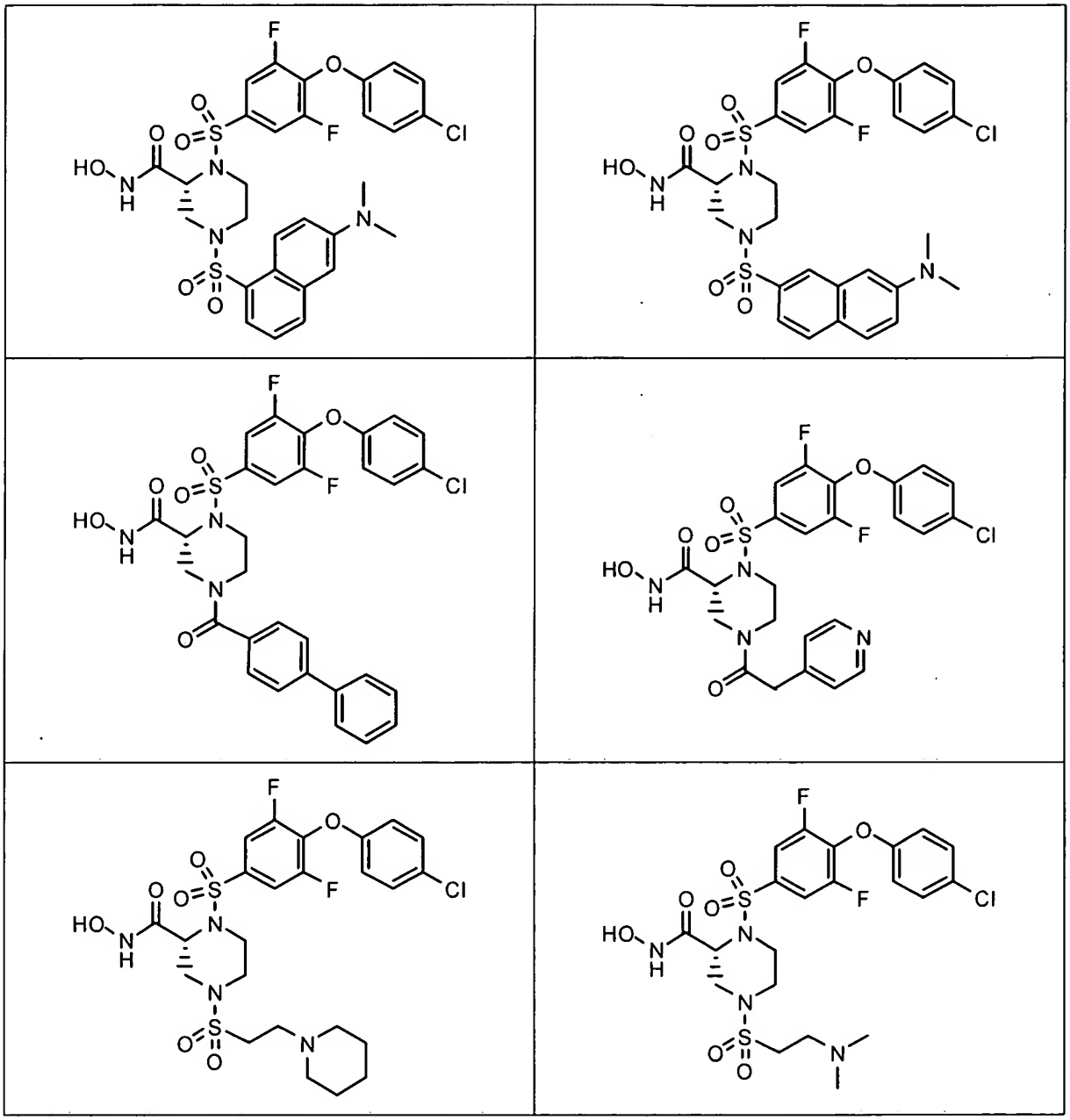


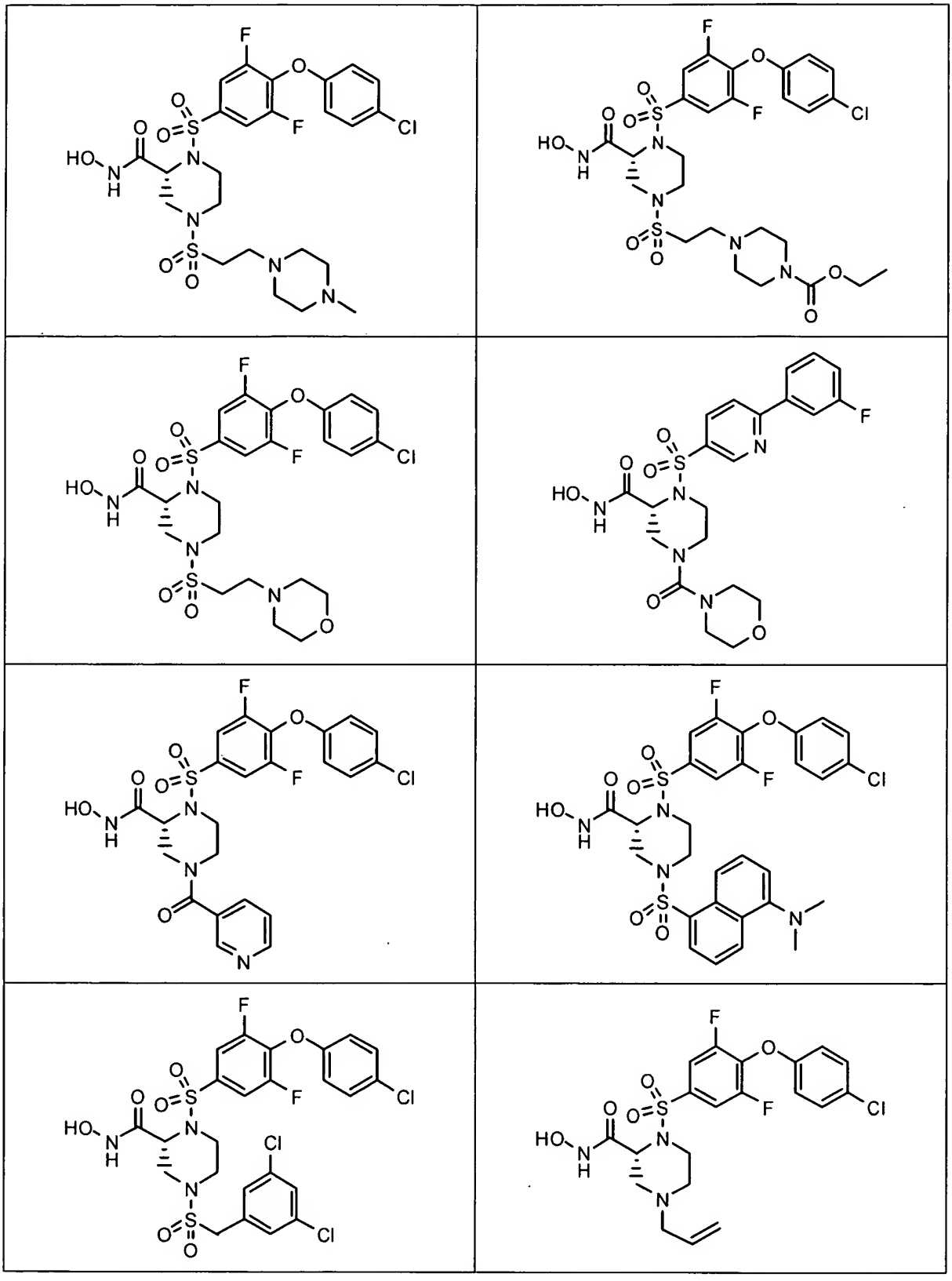


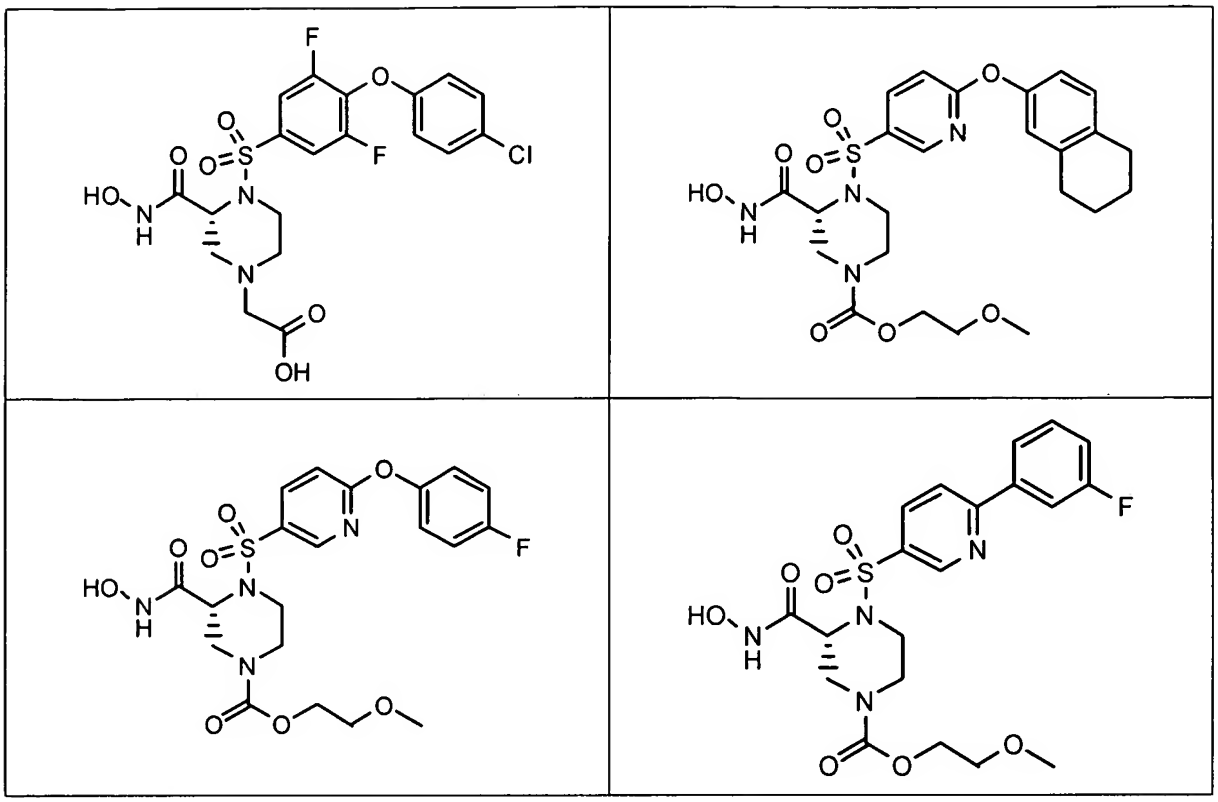




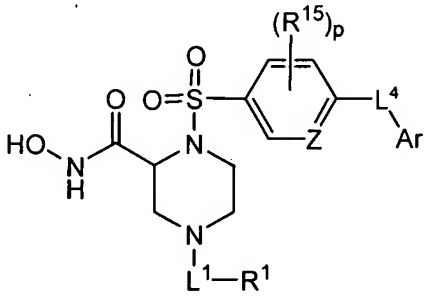








15. (original) A compound according to formula **IV**,



IV

and pharmaceutically acceptable salts, esters, amides, and prodrugs thereof wherein,

Z is $-C(R^{15})=$, $-C(H)=$, or $-N=$;

Ar is aryl or heteroaryl, each optionally substituted;

R^{15} is fluoro;

p is 0, 1, 2, or 3;

L^1 is $-C(O)-$, $-S(O)_2-$, or $-(CH_2)_n-$;

L^4 is nothing or -O-;

R^1 is –H, $-OR^{11}$, $-(CH_2)_nR^{11}$, $-C(O)R^{11}$, or $-NR^{12}R^{13}$;

R^{11}, R^{12}, and R^{13} independently are

d) R^{50};

e) saturated or mono- or poly- unsaturated C_5-C_{14}-mono- or fused poly-cyclic hydrocarbyl, optionally containing one or two annular heteroatoms per ring and optionally substituted with one or two R^{50} substituents;

f) C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, or -C(O)H, each of which is optionally substituted with one, two or three substituents independently selected from R^{50} and saturated or mono- or poly- unsaturated C_5-C_{14}-mono- or fused poly- cyclic hydrocarbyl, optionally containing one or two annular heteroatoms per ring and optionally substituted with one, two or three R^{50} substituents;

or R^{12} and R^{13} together with the N to which they are covalently bound, a C_5-C_6 heterocycle optionally containing a second annular heteroatom and optionally substituted with one or two R^{50} substituents; and

R^{50} is R^{51}-L^3-$(CH_2)_n$-;

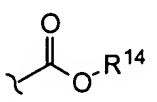
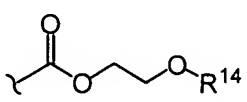
L^3 is -O-, -NH-, $-S(O)_{0-2}$-, -C(O)-, -C(O)O-, -C(O)NH-, -OC(O)-, -NHC(O)-, $-C_6H_4$-, or a direct bond;

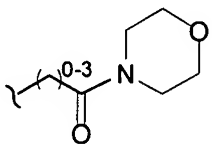
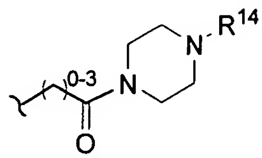
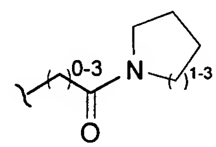
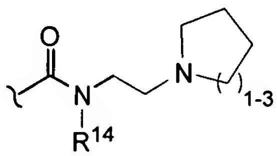
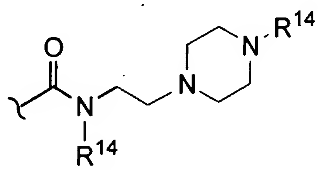
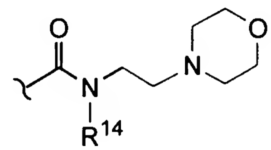
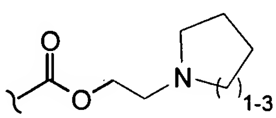
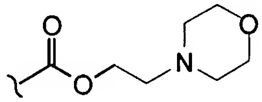
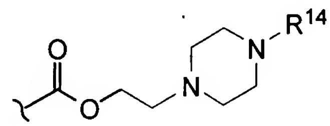
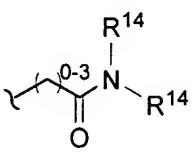
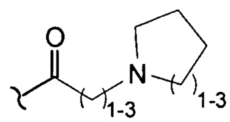
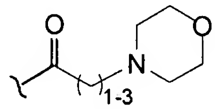
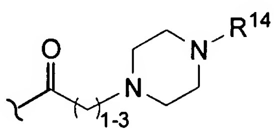
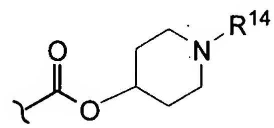
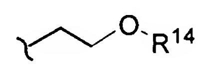
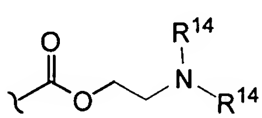
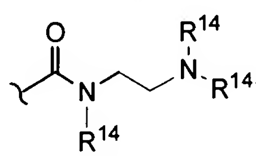
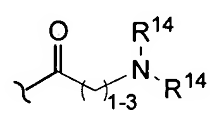
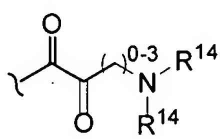
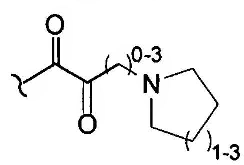
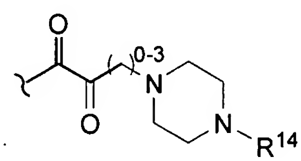
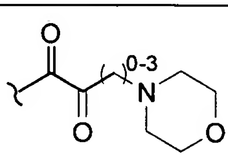
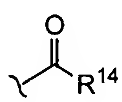
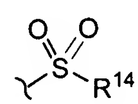
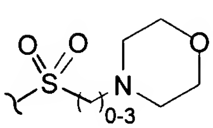
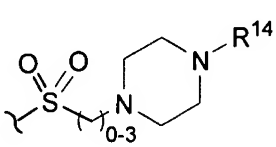
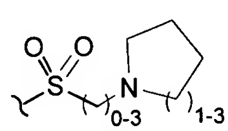
R^{51} is -H, C_1-C_6-alkyl, C_2-C_6-alkenyl, C_2-C_6-alkynyl, halo, $-CF_3$, $-OCF_3$, -OH, $-NH_2$, mono-C_1-C_6alkyl amino, di-C_1-C_6alkyl amino, -SH, $-CO_2H$, -CN, $-NO_2$, $-SO_3H$, or a saturated or mono- or poly- unsaturated C_5-C_{14}-mono- or fused poly- cyclic hydrocarbyl, optionally containing one or two annular heteroatoms per ring and optionally substituted with one, two, or three substituents;

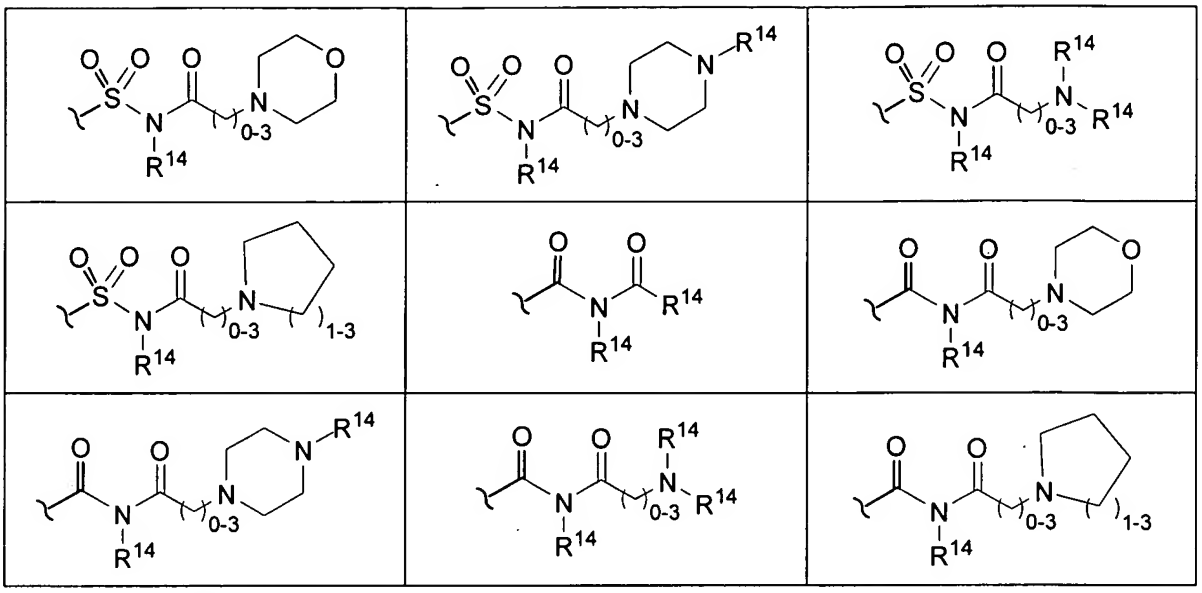
wherein n is 0, 1, 2, or 3;

provided that an O or S is not singly bonded to another O or S in a chain of atoms.

16. (original) The compound according to claim 15, wherein $-L^1-R^1$ is selected from:

$-R^{14}$		



wherein each R^{14} is independently selected from –H, $-(CH_2)_{1-3}CO_2H$, alkyl, alkoxy, alkenyl, aryl, heteroaryl, arylalkyl, and heteroarylalkyl.

17. (original) The compound according to claim 16, wherein Z is $-C(R^{15})=$ or –C(H)=; L^4 is -O-; and p is at least one.

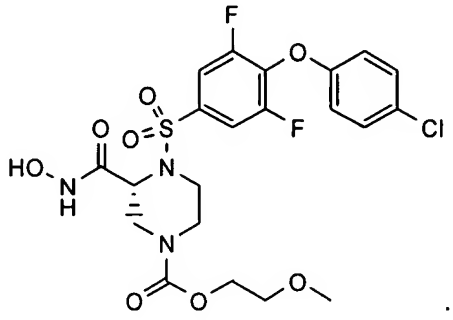
18. (original) The compound according to claim 17, wherein Ar is selected from the group consisting of phenyl, biphenyl, napthyl, tetrahydronaphthalene, chromen-2-one, dibenzofuran, pyryl, furyl, pyridyl, 1,2,4-thiadiazolyl, pyrimidyl, thienyl, isothiazolyl, imidazolyl, tetrazolyl, pyrazinyl, pyrimidyl, quinolyl, isoquinolyl, benzothienyl, isobenzofuryl, pyrazolyl, indolyl, purinyl, carbazolyl, benzimidazolyl, and isoxazolyl, each optionally substituted.

19. (original) The compound according to claim 18, wherein Ar is phenyl, optionally substituted, with at least one halogen.

20. (original) The compound according to claim 19, wherein p is at least two.

21. (original) The compound according to claim 20, wherein $-L^1-R^1$ is $-C(=O)OR^{14}$ or $-(CH_2)_2OR^{14}$.

22. (original) The compound according to claim 21, having the structure:



23. (original) The compound according to claim 16, wherein Z is –N=; and L^4 is -O-.

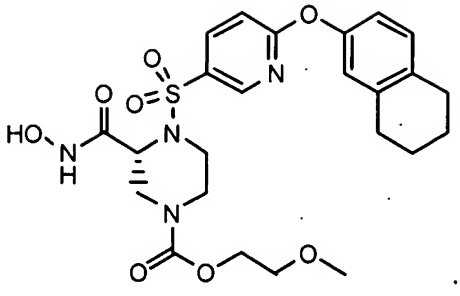
24. (original) The compound according to claim 23, wherein Ar is selected from the group consisting of phenyl, biphenyl, napthyl, tetrahydronaphthalene, chromen-2-one, dibenzofuran, pyryl, furyl, pyridyl, 1,2,4-thiadiazolyl, pyrimidyl, thienyl, isothiazolyl, imidazolyl, tetrazolyl, pyrazinyl, pyrimidyl, quinolyl, isoquinolyl, benzothienyl, isobenzofuryl, pyrazolyl, indolyl, purinyl, carbazolyl, benzimidazolyl, and isoxazolyl, each optionally substituted.

25. (original) The compound according to claim 24, wherein Ar is optionally substituted tetrahydro-naphthalene.

26. (original) The compound according to claim 25, wherein $-L^1-R^1$ is $-C(=O)OR^{14}$ or $-(CH_2)_{2-3}OR^{14}$.

27. (original) The compound according to claim 26, wherein p is zero.

28. (original) The compound according to claim 27, having the structure:



29. (original) The compound according to claim 16, wherein Z is –N=; and L^4 is nothing.

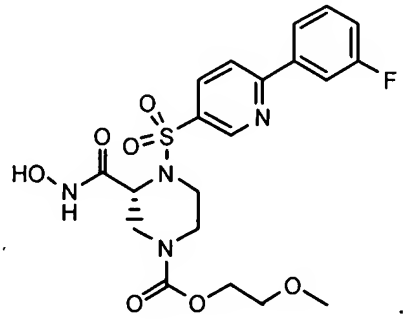
30. (original) The compound according to claim 29, wherein Ar is selected from the group consisting of phenyl, biphenyl, napthyl, tetrahydronaphthalene, chromen-2-one, dibenzofuran, pyryl, furyl, pyridyl, 1,2,4-thiadiazolyl, pyrimidyl, thienyl, isothiazolyl, imidazolyl, tetrazolyl, pyrazinyl, pyrimidyl, quinolyl, isoquinolyl, benzothienyl, isobenzofuryl, pyrazolyl, indolyl, purinyl, carbazolyl, benzimidazolyl, and isoxazolyl, each optionally substituted.

31. (original) The compound according to claim 30, wherein p is zero.

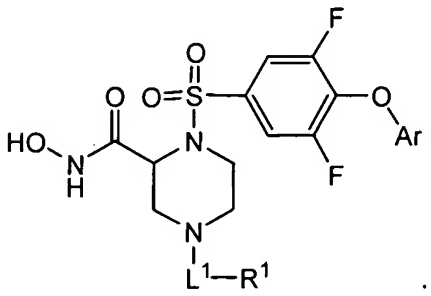
32. (original) The compound according to claim 31, wherein Ar is optionally substituted phenyl.

33. (original) The compound according to claim 32, wherein $-L^1-R^1$ is $-C(=O)OR^{14}$ or $-(CH_2)_{2-3}OR^{14}$.

34. (original) The compound according to claim 33, having the structure:



35. (original) The compound according to claim 16, of formula **V**,

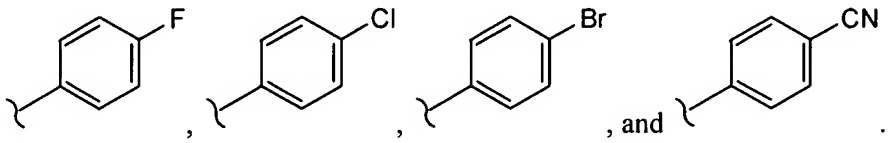


V

36. (original) The compound according to claim 35, wherein Ar is selected from the group consisting of phenyl, biphenyl, napthyl, tetrahydronaphthalene, chromen-2-one, dibenzofuran, pyryl, furyl, pyridyl, 1,2,4-thiadiazolyl, pyrimidyl, thienyl, isothiazolyl, imidazolyl, tetrazolyl, pyrazinyl, pyrimidyl, quinolyl, isoquinolyl, benzothienyl, isobenzofuryl, pyrazolyl, indolyl, purinyl, carbazolyl, benzimidazolyl, and isoxazolyl, each optionally substituted.

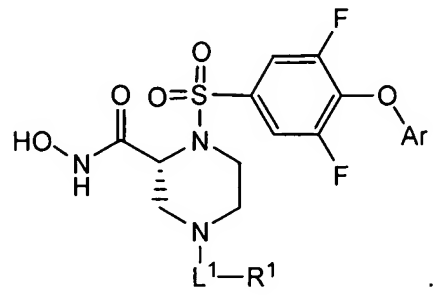
37. (original) The compound according to claim 36, wherein Ar is phenyl, optionally substituted, with at least one halogen.

38. (original) The compound according to claim 36, wherein Ar is selected from,



, and .

39. (original) The compound according to claim 37, wherein the absolute stereochemistry is according to formula **VI**,



VI

40. (original) The compound according to claim 39, wherein $-L^1-R^1$ is $-C(=O)OR^{14}$ or $-(CH_2)_{2-3}OR^{14}$.

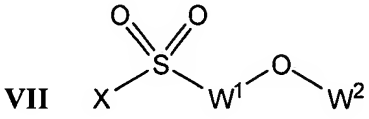
41. (cancelled)

~~51~~ 42. (currently amended) A pharmaceutical composition comprising a compound as described in ~~any of~~ claims 1 ~~-51~~ and a pharmaceutically acceptable carrier.

~~52~~ 43. (currently amended) A method of treating cancer, arthritis, and diseases related to angiogenesis comprising administering to a mammal in need of such treatment a therapeutically effective amount of a pharmaceutical composition according to claim ~~51~~ 42.

~~53~~ 44. (currently amended) A method of modulating the activity of Adam-10 comprising administering to a mammal in need of such treatment a therapeutically effective amount of a pharmaceutical composition according to claim ~~51~~ 42.

~~54~~ 45. (currently amended) A method of making a bis-aryl ether sulfonyl halide according to formula **VII**:

VII 

wherein X is a halide; and W^1 and W^2 are each independently an optionally substituted aryl, the method comprising: (a) combining a metal-aryloxide salt of a corresponding hydroxide-substituted aryl compound with a fluoro-substituted nitro aryl compound to make a bis-aryl ether nitro-aromatic compound; (b) reducing a nitro group of the bis-aryl ether nitro-aromatic compound to produce a corresponding aniline derivative; and (c) converting the corresponding aniline derivative to the bis-aryl ether sulfonyl halide.

~~55~~ 46. (currently amended) The method of claim ~~54~~ 45, wherein (a) – (c) are performed in the order described.

~~56~~ 47. (currently amended) The method of claim ~~55~~ 46, wherein the metal-aryloxide salt is combined with the fluoro-substituted nitro aryl in an organic solvent.

~~57~~ 48. (currently amended) The method of claim ~~56~~ 47, wherein the organic solvent comprises at least one of DMF and acetonitrile.

~~58~~ 49. (currently amended) The method of claim ~~57~~ 48, wherein the metal-aryloxide salt comprises at least one of a cesium salt and a potassium salt.

~~59~~ 50. (currently amended) The method of claim ~~58~~ 49, wherein the corresponding aniline derivative is converted to the bis-aryl ether sulfonyl halide via a diazonium intermediate of said corresponding aniline derivative.

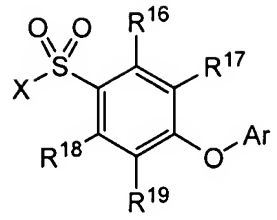
~~60~~ 51. (currently amended) The method of claim ~~59~~ 50, wherein the fluoro-substituted nitro aryl compound is 3,4,5-trifluornitrobenzene.

~~61~~ 52. (currently amended) The method of claim ~~60~~ 51, wherein the metal-aryloxide salt is a cesium salt.

~~62~~ 53. (currently amended) The method of claim ~~61~~ 52, wherein the corresponding hydroxide-substituted aryl compound is 4-chlorophenol.

~~63~~ 54. (currently amended) The method of claim ~~62~~ 53, wherein the bis-aryl ether sulfonyl halide is 4-(4-chlorophenoxy)-3,5-difluorophenylsulfonyl chloride.

~~64~~ 55. (currently amended) A sulfonyl halide according to formula **VIII**:



VIII

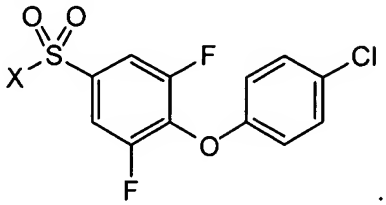
wherein X is halogen; R^{16}, R^{17}, R^{18}, and R^{19},are each independently either –H or –F; and Ar is aryl or heteroaryl, each optionally substituted.

~~65~~ 56. (currently amended) The sulfonyl halide of claim ~~64~~ 55, wherein R^{16} and R^{18} are each –H; and R^{17} and R^{19} are each –F.

~~66~~ 57. (currently amended) The sulfonyl halide of claim ~~65~~ 56, wherein Ar is selected from the group consisting of phenyl, biphenyl, napthyl, tetrahydronaphthalene, chromen-2-one, dibenzofuran, pyryl, furyl, pyridyl, 1,2,4-thiadiazolyl, pyrimidyl, thienyl, isothiazolyl, imidazolyl, tetrazolyl, pyrazinyl, pyrimidyl, quinolyl, isoquinolyl, benzothienyl, isobenzofuryl, pyrazolyl, indolyl, purinyl, carbazolyl, benzimidazolyl, and isoxazolyl, each optionally substituted.

~~67~~ 58. (currently amended) The sulfonyl halide of claim ~~66~~ 57, wherein Ar is phenyl, optionally substituted, with at least one halogen.

~~68~~ 59. (currently amended) The sulfonyl halide of claim ~~67~~ 58, of formula **IX**:



IX

~~69~~ 60. (currently amended) The sulfonyl halide of claim ~~68~~ 59, wherein X is -Cl.